

PEDIATRIC ASTHMA (NOT JUST LITTLE ADULTS)

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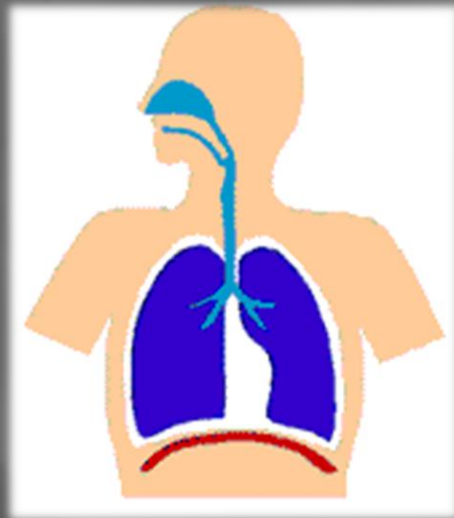


**Family Allergy
& Asthma Care**
of Montana



Disclosures

- ▣ Speaker's Bureau: TEVA, Merck
- ▣ I will be including information “off label”
- ▣ NHLBI asthma recommendations vs. package insert



Goals

- ▣ Review risk factors for developing asthma as child
- ▣ How to evaluate infants and toddlers with suspected asthma.
- ▣ How to treat infants and toddlers with asthma according to evidence-based treatment guidelines and accepted standards
- ▣ How pediatric asthma is different from adult asthma

Pediatric Asthma ?

Infants/young children <3 yr

Wheeze

Once



Bronchiolitis

Evaluation: GER, anatomic

Management

Recurrent
≥4 episodes
Improve with
asthma meds



Asthma

Modified API

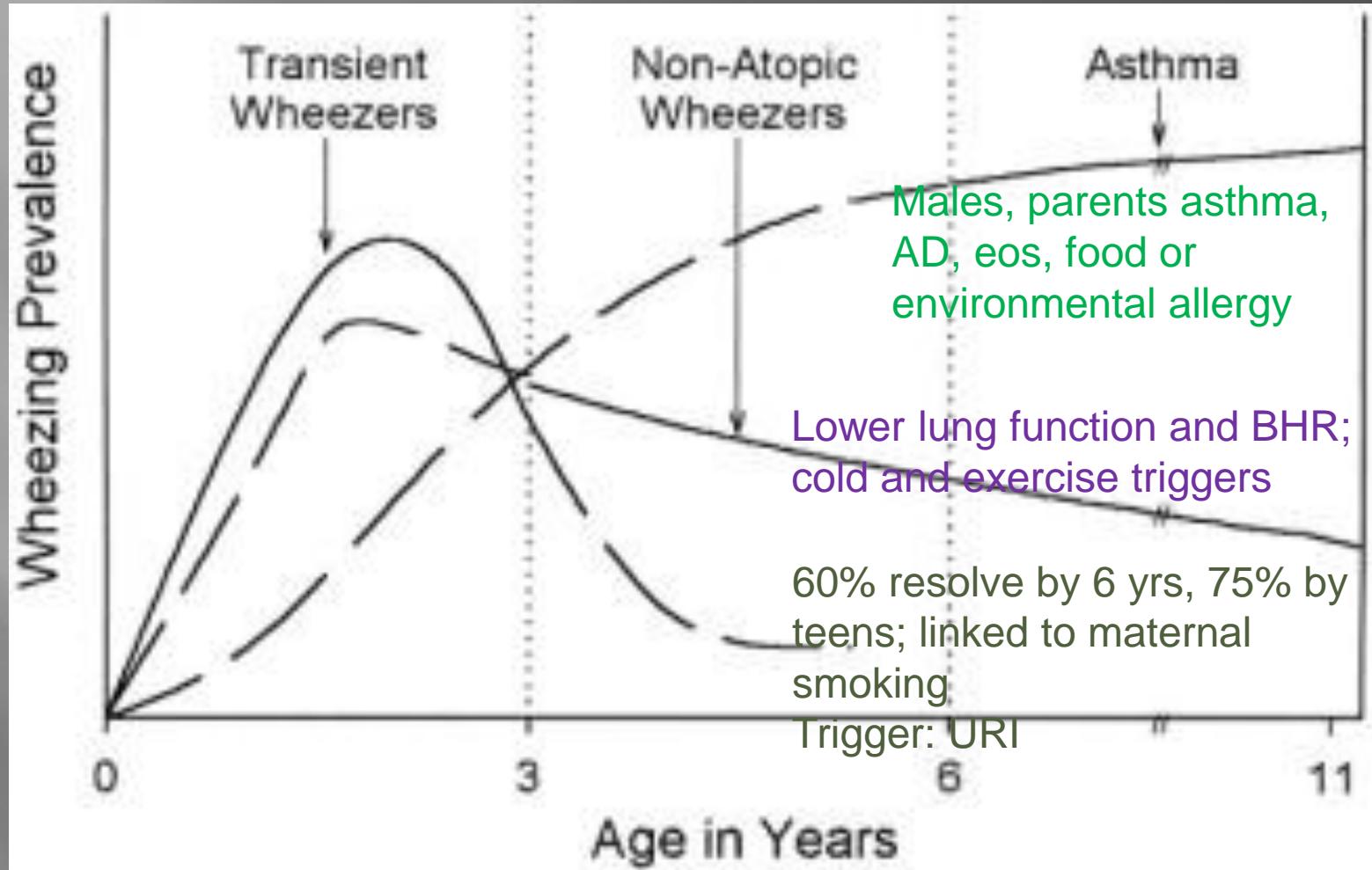


Transient



Persistent

Pediatric Wheezing Phenotypes: Natural History



Hypothetical peak prevalence by age for 3 different wheezing phenotypes. Prevalence for each age interval should be the area under the curve. This does not imply that the groups are exclusive. (Modification [with permission] of [Figure 2](#) in: Stein RT, et al. Peak flow variability, methacholine responsiveness and atopy as markers for detecting different wheezing phenotypes in childhood. *Thorax* 1997;52:946-52)

Modified Asthma Predictive Index

- ▣ 4 or more wheezing episodes (1 MD dx)

And

- ▣ 1 major or 2 minor criteria

- ▣ **Major**

- Parental history of asthma
- Atopic dermatitis
- Aeroallergen sensitization

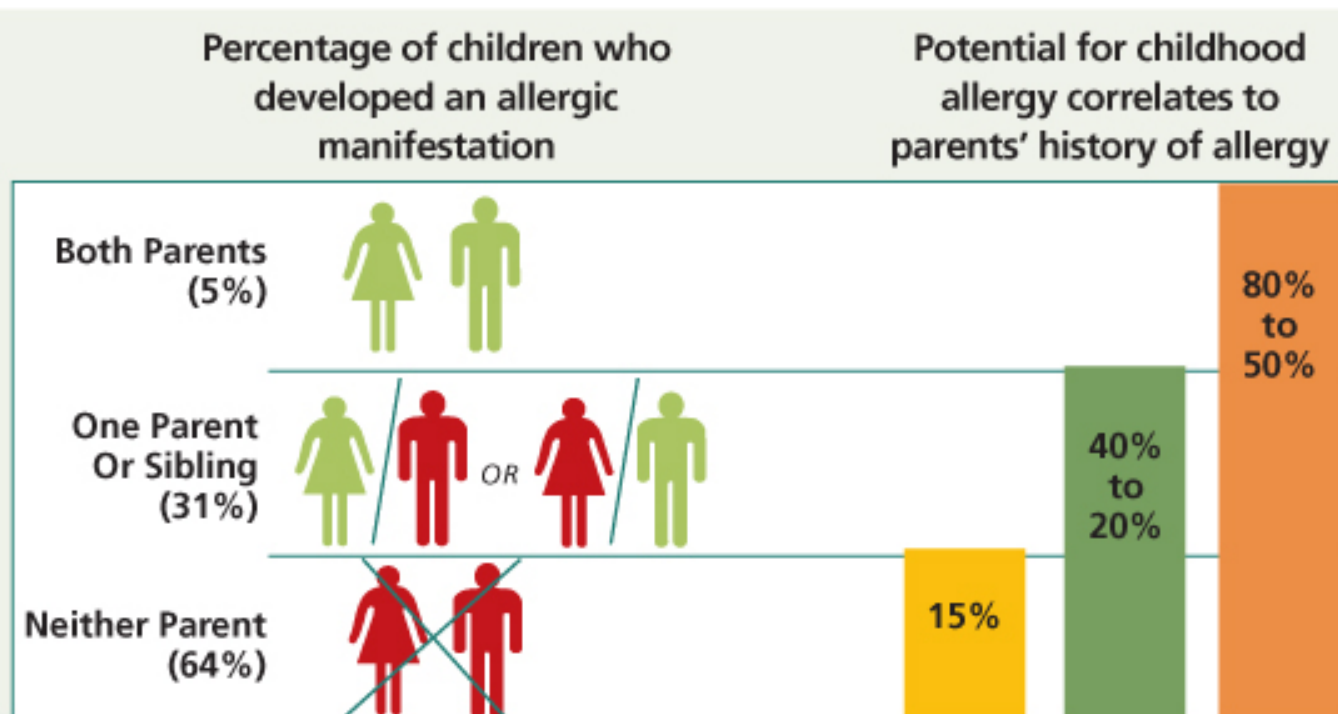
- ▣ **Minor**

- Food allergy: milk, egg, or peanut
- Wheezing unrelated to cold
- Blood eosinophilia $\geq 4\%$
- MD dx of AR

Negative mAPI in first 3 yrs of life is 95% accurate to predict those without asthma between ages 6-13 yr old

Role of Family History

FIGURE 1. Family History and Potential for Childhood Allergy



Adapted from Exl BM. *Nutr Res.* 2001;21:355-379.

Lung Development: Stages

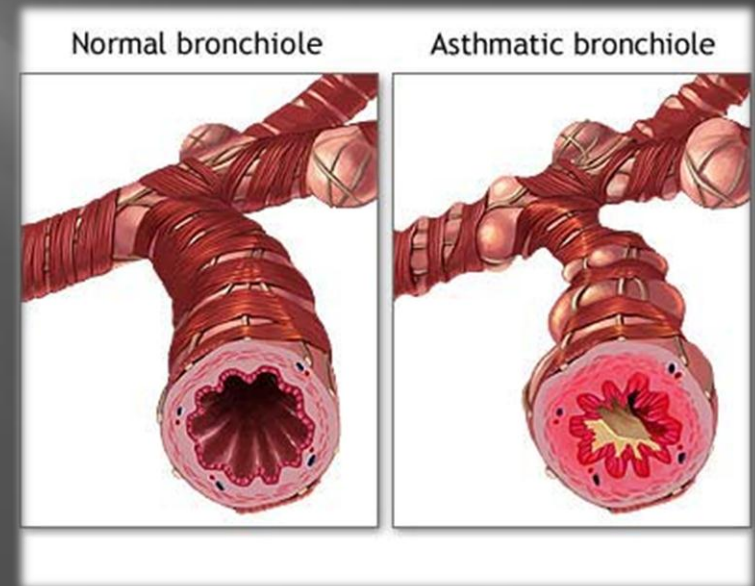
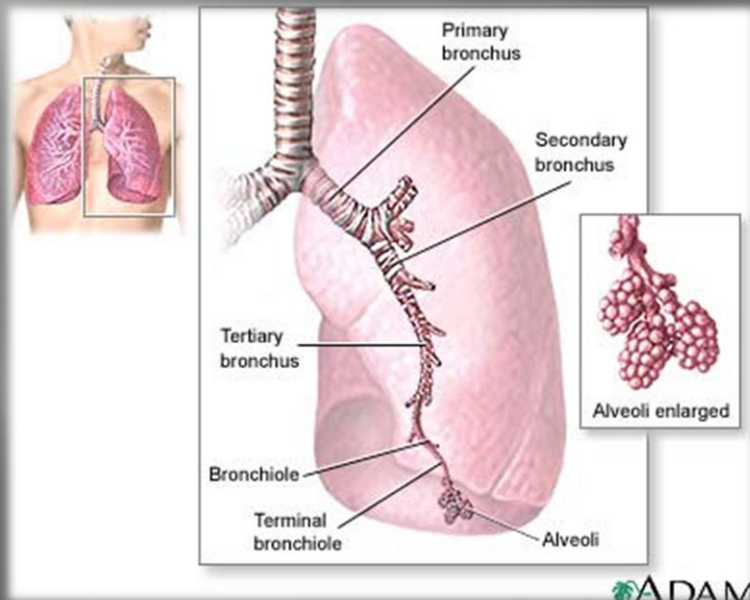
- ▣ **Embryonic:** 3 to 7 wks after fertilization
 - Lung sacs develop from ventral wall of esophagus
- ▣ **Pseudoglandular:** 15-17 wk
 - Bronchial tree develops as solid tubes that bud
- ▣ **Canalicular:** 16-26 wks
 - Lumens begin to form, pneumocyte differentiation
 - Capillaries arrange around bronchials
- ▣ **Saccal:** 24-38 wks
 - Formation of alveolar ducts, air sacs and alveoli
- ▣ **Most alveoli develop after birth!**
 - Lung volume doubles at 6 mo and triples at 1 yr

Differential Diagnosis: Wheezing in Infancy

- ▣ Upper Airway
 - FB, VCD-paralysis, laryngotracheomalacia, laryngeal web, papilloma subglottic stenosis, hemangioma
- ▣ Lower airway
 - Asthma/Foreign body, bronchial stenosis-malacia, lobar emphysema
- ▣ Infectious/Post-Infectious
 - Epiglottitis, croup, tracheitis, bronchiolitis, Diphtheria, Chlamydia, Pneumocystis, Histoplasma, bronchiectasis, Pertussis, Retropharyngeal abscess, bronchiolitis obliterans
- ▣ Compression Syndrome
 - TB, adenopathy, vascular ring, pulmonary sling, mediastinal mass, congenital goiter, teratoma, aspiration syndromes
- ▣ Congenital Disorders
 - CF, TE-fistula, ciliary dyskinesia, immune deficiency, D-hernia, CLD of prematurity, pulm lymphangiectasia, heart disease
- ▣ Other
 - GE reflux, Munchausen by proxy, neurofibroma, pulm histiocytosis

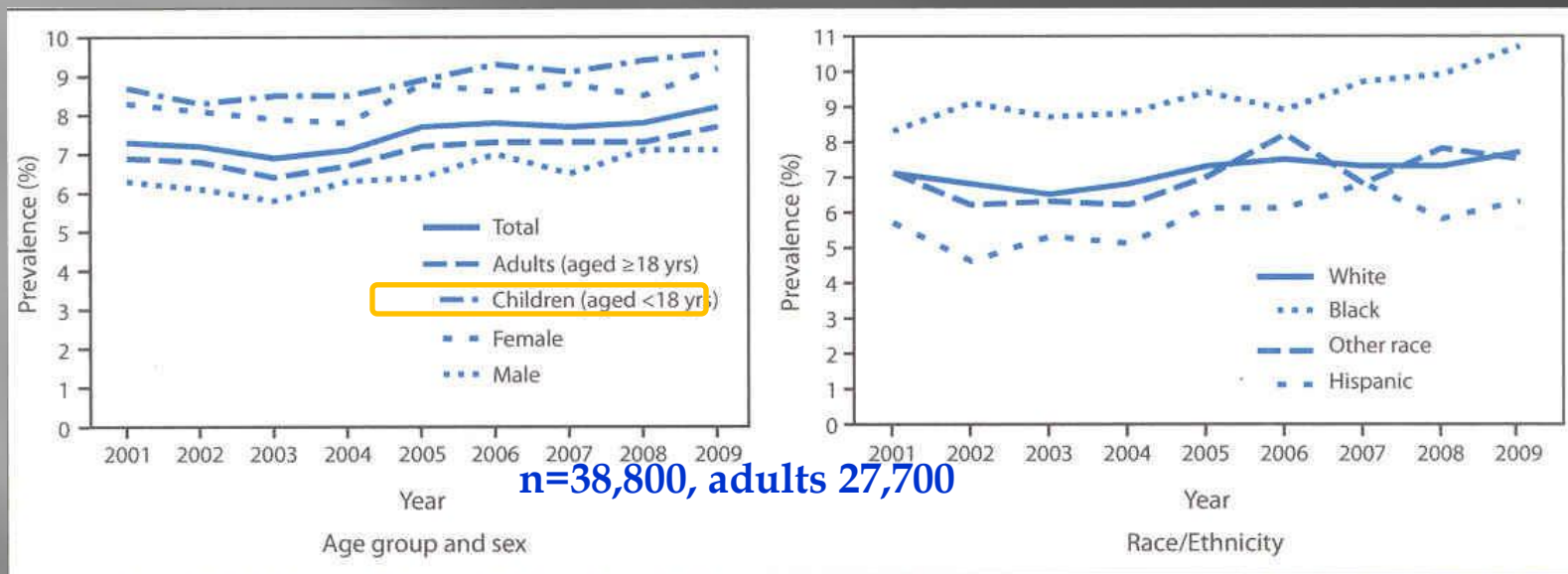
Asthma is.....

- ▣ Lung Disorder: recognized in 1698
 - Periodic/persistent: cough, wheeze, dyspnea
 - Airway inflammation (eos)
 - Bronchial hyper-reactivity
 - Bronchoconstriction



Asthma: Still a problem in U.S.

Vital signs: Asthma Prevalence, Disease Characteristics and self management Education—US, 2001-2009 CDC, MMWR, Vol 60, May 3, 2011



Asthma up despite better air quality & less smoking.

In 2008:

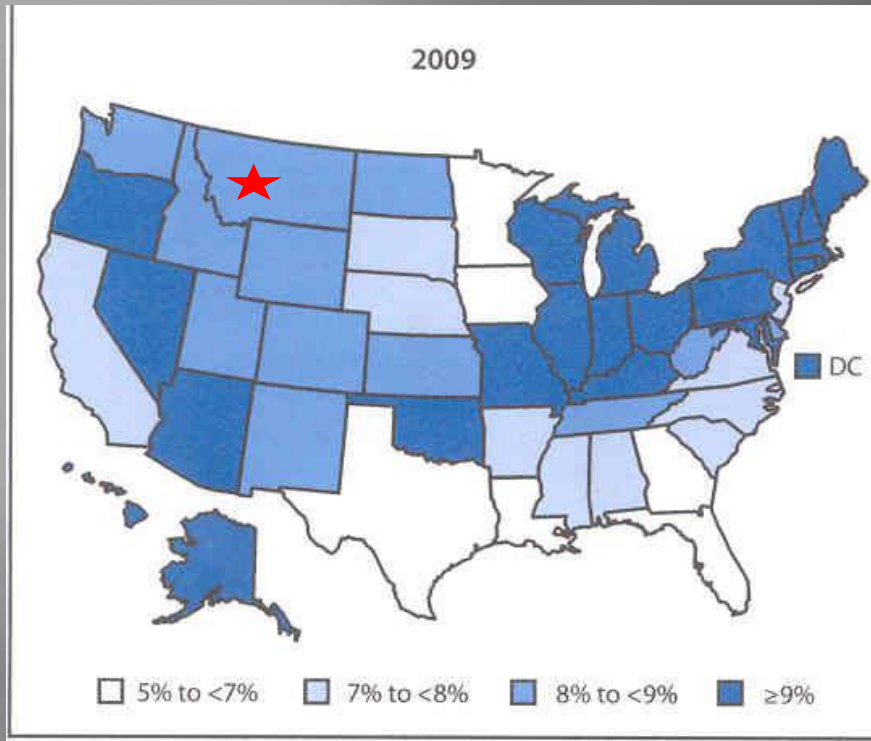
1/2 of asthmatics had attack in last year

1/3 had action plan

1/2 given environmental control

Most common chronic disease of childhood.

Montana



CDC: Prevalence of asthma in adults

Behavioral Risk Factor Surveillance System
(phone survey for all 50 states; CDC)

By the Numbers

- 84,000 people have asthma
- 34% of kids uncontrolled asthma
- 60%: limits activities
- 65% don't know signs/sx's
- 75% don't know how to respond to an attack
- 25% have written action plan
- 10% of kids have good inhaler technique
- Cost in 2010:
 - \$8k/hosp and \$900/ED in hospital stays



Asthma: Pediatric vs. Adult

▣ Pediatric asthma...

- Natural history: not fully understood
- Evaluation complicated: difficulty in obtaining lung function and biomarkers
- Multiple wheezing phenotypes expressed early in childhood
- Longitudinal data are lacking
- Asthma may impact lung growth
- Smaller airway size/flow rates impact med deposition
- Most effective therapy for each phenotype ?
- Diagnosis of exclusion in <1 yr olds

Risk Factors for Asthma

- ▣ Acetaminophen
 - ▣ Paracetamol in Pregnancy and Risk of Wheezing in Offspring: Meta-Analysis Clin Exp Allergy 2011;41:482
 - ▣ 6 studies (5 prospective cohort, 1 cross section) ages 30-84 months
 - ▣ Results: odds ratio 1.21 (95% CI 1.02-1.44)
 - ▣ Conc: increased risk of childhood asthma
- ▣ Prematurity
 - ▣ Natl Cohort Study Sweden (Pediatr 2011;127)
 - ▣ Extreme pre-term birth 23-27 wks is associated in OR 2.4 for asthma
 - ▣ AJRCCM 2010
 - ▣ <25 wk pre-term
 - ▣ 25% had current asthma at 11 yrs old vs. 13% (term)

Risk Factors for Asthma

▣ Viral infections

▣ Rhinovirus (Ped Allergy Immunol 2010;1008)

- ▣ Children hospitalized with RV induced wheezing had OR 3.5 for allergen sensitization

▣ RSV (Chest 2010;138:338)

- ▣ Severe RSV in twins, 1 hospitalized at 10 mo. At 7 yrs, asthma prevalence was 18% and no different b/w groups
- ▣ No specific viral effect/? genetic

▣ Bacterial Infections

▣ (Bisgaard, BMJ 2010;341)

- ▣ N=411 infants,
- ▣ 4 wks to 3 yrs old

▣ Viral and bacterial

▣ Results:

- ▣ Wheezy episodes associated with virus and Strep pneumo, H influenza, Moraxella catarrhalis

Determinants in Childhood Asthma

- ▣ Age
 - Atopic infants---more likely to have asthma
 - Non-atopic infants----less likely
 - Earlier age predicts relapse of wheeze as adult
- ▣ Severity of Onset
 - Initial severity and long-term prognosis: ??
- ▣ Family History
 - Increased risk with Mom or Dad with asthma
- ▣ Smoking
 - Second hand smoke: linked to asthma sx's
 - In utero exposure: low lung function, wheeze

Determinants in Childhood Asthma

▣ Atopic Status

- Allergic sensitization-----poorer asthma prognosis
 - 29% of 1-2 y/o were SPT+ pollen
 - 40% of childhood asthmatics 1-3 y/o are SPT+ pollen
 - 52% of “ “ “ <3 y/o “ “ “
- Persistence of eczema----asthma persistence
- Having eczema, eosinophilia, rhinitis or +SPT ---- persistent wheezing (Modified API)
- Food allergic---more severe asthma
- Dust mite allergic---predicts development of asthma and persistence of asthma

▣ Gender

- Boys—more asthma in school age
- Girls—more persistent asthma into adulthood

Determinants in Childhood Asthma

▣ Lung function

- Diminished lung function predicts wheezing during the first 3 yrs
- If lung function declines during the first 6 yrs, linked to persistent wheezing
- Lung function in children predicts lung fxn in adults

▣ Treatment

- Current treatment of asthma (even early and intensive) do not change the natural history of asthma

Evaluation: Wheezing

▣ History

- Sudden onset-----FB
- Intubation at birth----stenosis
- Premie-----CLD-prematurity
- Pneumonia-----aspiration, TEF, CF, HIV, PID
- Formula change---allergy
- Isolated episode-----TB, RSV, Adeno, Histo, Parainfluenza, metapneumo-
- Response to SABA or steroids
- ED visits/Hospitalization

▣ Examination

- Stridor, inspiratory wheeze, rale/rhonchi, cardiac, rash

▣ Chest x-ray

▣ Spirometry: >5 yr; FeNO Lung inflammation: >7 yr

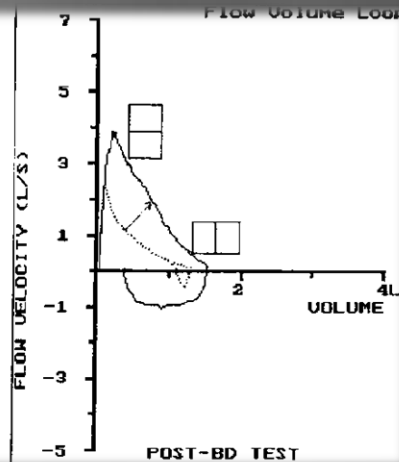
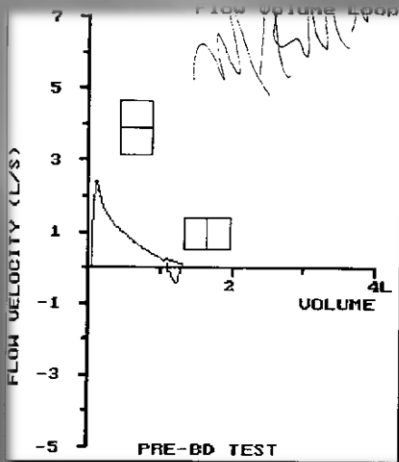
▣ Allergy Testing: > 1 yr old

▣ Other: UGI, pH probe, swallow study, Sweat Cl, bronch/bx, CBC, Qlgs

Spirometry & FeNO



- ▣ Spirometry
 - FEV1=small airways
- ▣ Peak Flows
 - Velocity in large airway
- ▣ FeNO (exhaled nitric oxide)
 - Direct measure of inflammation
- ▣ Pulse oximetry
 - Hypoxemia is late finding in asthma



Asthma Severity



Mild



Moderate



Severe



Classifying Asthma Severity: Impairment


| Components of Severity | | Classification of Asthma Severity | | | |
|---|--|---|--|---|---|
| | | Intermittent | Persistent | | |
| | | | Mild | Moderate | Severe |
| Symptoms | | ≤2 d/wk | >2 d/wk | Daily | through day |
| Nighttime awakening | | 0 ≤2x/mo ≤2x/mo | 1–2x/mo 3–4x/mo 3–4x/mo | 3–4x/mo >1x/wk; no nightly >1x/wk; no nightly | >1x/wk Often 7x/wk Often 7x/wk |
| Short-acting β_2 -agonist for symptoms <u>not</u> EIB prevention | | ≤2 d/wk | >2 d/wk; not daily >2 d/wk; not daily >2 d/wk; not >1x/d | Daily | Several times per day |
| Interfere with nl activity | | None | Minor limitation | Some limitation | Extremely limited |
| Lung function Normal FEV ₁ /FVC: 8–19 y 85% 20–39 y 80% 40–59 y 75% 60–80 y 70% | | <ul style="list-style-type: none"> • Normal FEV₁ between attacks • FEV₁ >80% of pred • FEV₁/FVC >85% • Normal FEV₁ between attacks • FEV₁ >80% of pred • FEV₁/FVC normal | <ul style="list-style-type: none"> • FEV₁ ≥80% pred • FEV₁/FVC >80% • FEV₁ >80% pred • FEV₁/FVC normal | <ul style="list-style-type: none"> • FEV₁ =60–80% pred • FEV₁/FVC =75–80% • FEV₁ 60 to 80% pred • FEV₁/FVC reduced 5% | <ul style="list-style-type: none"> • FEV₁ <60% pred • FEV₁/FVC <75% • FEV₁ <60% pred • FEV₁/FVC reduced >5% |

- Recommended for all age groups
- Children ≤4 y
- Children 5–11 y
- Persons ≥12 y

^aEIB=exercise-induced bronchoconstriction.

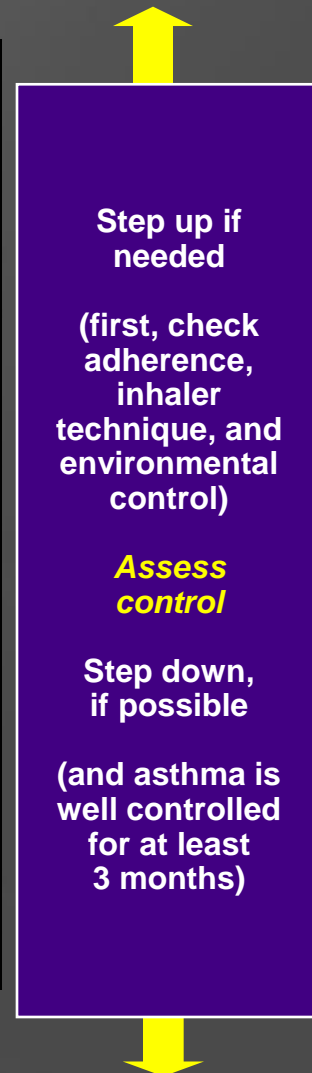
Adapted from NAEPP, NHLBI, NIH. Expert Panel Report 3:

Guidelines for the Diagnosis and Management of Asthma. August 2007.

| Components of Severity | | Classification of Asthma Severity (0–4 years of age) | | | |
|---|---|--|--|---|-----------------------|
| | | Intermittent | Persistent | | |
| | | | Mild | Moderate | Severe |
| Impairment | Symptoms | ≤2 days/week | >2 days/week but not daily | Daily | Throughout the day |
| | Nighttime awakenings | 0 | 1–2x/month | 3–4x/month | >1x/week |
| | Short-acting beta ₂ -agonist use for symptom control (not prevention of EIB) | ≤2 days/week | >2 days/week but not daily | Daily | Several times per day |
| | Interference with normal activity | None | Minor limitation | Some limitation | Extremely limited |
| <div><div>Risk</div><div></div></div> | Exacerbations (consider frequency and severity) | 0–1/year | ≥2 exacerbations in 6 months requiring oral steroids, or ≥4 wheezing episodes/1 year lasting >1 day AND risk factors for persistent asthma | | |
| | | Frequency and severity may fluctuate over time Exacerbations of any severity may occur in patients in any severity category | | | |
| Recommended Step for Initiating Therapy (See figure 4-1a for treatment steps.) | | Step 1 | Step 2 | Step 3 and consider short course of oral steroids | |
| | | In 2–6 weeks, depending on severity, evaluate level of asthma control achieved. If no clear benefit in 4–6 weeks, consider adjusting therapy or alternative diagnoses. | | | |

Managing Asthma in Children ≤4 yrs

| Recommended Step for Initiating Treatment | | Classification of Asthma Severity | | | |
|--|--|-----------------------------------|---|--|--|
| | | Intermittent | Persistent | | |
| | | | Mild | Moderate | Severe |
| | | | Step 1 | Step 2 | Step 3 |
| Intermittent Asthma | Persistent Asthma: Daily Medication Consult with asthma specialist if step-3 or higher is required. Consider consultation at step 2. | | | | |
| Step 1 | Step 2 | Step 3 | Step 4 | Step 5 | Step 6 |
| Preferred: SABA prn | Preferred: low-dose ICS Alternative: cromolyn or montelukast | Preferred: medium-dose ICS | Preferred: medium-dose ICS + either LABA or montelukast | Preferred: High-dose ICS + either LABA or montelukast | Preferred: high-dose ICS + either LABA or montelukast Oral steroids |
| Patient Education and Environmental Control at Each Step | | | | | |
| Quick-Relief Medication for All Patients | | | | | |



Asthma Control for Children 0-4 yrs old

| Components of Control | | Classification of Asthma Control (≤ 4 yr old) | | |
|----------------------------------|--|--|---------------------------|-----------------------------------|
| | | Well controlled | Not well controlled | Very poorly controlled |
| Impairment | Symptoms | ≤ 2 days/week | > 2 days/week | Throughout day |
| | Nighttime awakens | 0-1x/month | > 1 x/month | > 1 x/wk |
| | Interferes with normal activity | None | Some limitation | Extremely limited |
| | Short-acting β_2 agonist for symptoms <u>not</u> EIB | ≤ 2 days/week | > 2 days/week | Several times per day |
| Risk | Attacks requiring oral steroids | 0-1/yr | 2-3x/yr | > 3 x/yr |
| | | Consider severity and interval since last exacerbation | | |
| | Treatment related adverse effects | Med side effects vary in intensity. | | |
| Recommended Action for treatment | | Maintain | Step up 1 and re-evaluate | Step up 1-2, pred and re-evaluate |

Adapted from NAEPP, NHLBI, NIH. *Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma*. August 2007

Managing Asthma in Children 5–11 Yrs

| Recommended Step for Initiating Treatment | | Classification of Asthma Severity | | | |
|--|---|---|--|---|--|
| | | Intermittent | Persistent | | |
| | | | Mild | Moderate | Severe |
| | | Step 1 | Step 2 | Step 3 | Step 3 or 4 |
| Intermittent Asthma | Persistent Asthma: Daily Medication Consult with asthma specialist if step-4 care or higher is required. Consider consultation at step 3. | | | | |
| Step 1 | Step 2 | Step 3 | Step 4 | Step 5 | Step 6 |
| Preferred: SABA prn | Preferred: low-dose ICS Alternative: cromolyn, LTRA, nedocromil, or theophylline | Preferred: EITHER: low-dose ICS + LABA, LTRA, or theophylline OR medium-dose ICS | Preferred: medium-dose ICS + LABA Alternative: medium-dose ICS + LTRA or theophylline | Preferred: high-dose ICS + LABA Alternative: high-dose ICS + either LTRA or theophylline | Preferred: high-dose ICS + LABA + oral steroid Alternative: high-dose ICS + LTRA or theophylline + oral steroid |
| Patient Education and Environmental Control at Each Step | | | | | |
| Steps 2–4: Consider SQ allergen immunotherapy for pts with allergic asthma | | | | | |
| Quick-Relief Medication for All Patients | | | | | |

Step up if needed
(first, check adherence, environment control, and comorbid conditions)

Assess control

Step down, if possible
(asthma is well controlled for at least 3 months)

Asthma Control for Children 5-11 yrs old

| Components of Control | | Classification of Asthma Control (5-11 yr old) | | |
|----------------------------------|--|--|---|----------------------------------|
| | | Well controlled | Not well controlled | Very poorly controlled |
| Impairment | Symptoms | ≤2 day/wk but not more than once a day | >2 days/wk or multiple times on ≤2 days/ week | Throughout the day |
| | Nighttime awakens | ≤1x/month | >2x/month | >2x/wk |
| | Interferes with normal activity | None | Some limitation | Extremely limited |
| | Short-acting β ₂ -agonist for symptoms <u>not</u> EIB | ≤2 d/wk | >2 days/wk | Several times per day |
| | FEV ₁ or peak flow FEV ₁ /FVC | ≥80% pred >80% | 60-80% pred 75-80% | <60% pred <75% |
| Risk | Attacks requiring oral steroids | 0-1/yr | ≥2/yr | |
| | | Consider severity and interval since last exacerbation | | |
| | Reduced lung growth | Evaluation requires long term follow up | | |
| | Treatment related adverse effects | Med side effects vary in intensity. | | |
| Recommended Action for treatment | | Maintain | Step up 1and re-evaluate | Step up1-2, pred and re-evaluate |

Childhood Asthma Control Test

Questions Completed by Child Age 4-11 Years

1. How is your asthma today?

SCORE



Very bad



Bad



Good



Very Good



2. How much of a problem is your asthma when you run, exercise or play sports?



It's a big problem, I can't do what I want to do.



It's a problem and I don't like it.



It's a little problem but it's okay.



It's not a problem.



3. Do you cough because of your asthma?



Yes, all of the time.



Yes, most of the time.



Yes, some of the time.



No, none of the time.



4. Do you wake up during the night because of your asthma?



Yes, all of the time.



Yes, most of the time.



Yes, some of the time.



No, none of the time.



Childhood Asthma Control Test

Questions Completed by Parent/Caregiver

5. During the last 4 weeks, on average, how many days per month did your child have any daytime asthma symptoms?

5

Not at all

4

1-3 days/mo

3

4-10 days/mo

2

11-18 days/mo

1

19-24 days/mo

0

Everyday

6. During the last 4 weeks, on average, how many days per month did your child wheeze during the day because of asthma?

5

Not at all

4

1-3 days/mo

3

4-10 days/mo

2

11-18 days/mo

1

19-24 days/mo

0

Everyday

7. During the last 4 weeks, on average, how many days per month did your child wake up during the night because of asthma?

5

Not at all

4

1-3 days/mo

3

4-10 days/mo

2

11-18 days/mo

1

19-24 days/mo

0

Everyday

TOTAL

Pediatric Asthma Management

- ▣ Avoidance
 - Irritants (smoke/wood stove): 13% of asthma <4 y/o
 - Allergens->1 yr (dust mite, cat, mouse, roach, grass)
 - Virus
- ▣ Medications
 - Quick relief vs. daily controller
- ▣ Allergy Injections
- ▣ Written asthma action plan
- ▣ Peak flows (+/-): >5 yr
- ▣ Annual influenza vaccine (6 mo)

Asthma Pharmacotherapy

Quick Reliever

SABA

Albuterol

Lev-albuterol

Pirbuterol MDI

Anticholinergic

Ipratropium*

Epinephrine

Oral steroid burst

1-2 mg/kg/day

Controller

Inhaled steroids

Long-acting beta agonist

Leukotriene modifiers

Montelukast: 6 mo-PAR, 1y

Allergen immunotherapy: 5 yr

Theophylline

~~Anti-IgE antibody: Xolair: 12 y~~

Cromolyn neb

~~Anticholinergic* (tiotropium)~~

Oral steroids

* Not FDA approved for asthma

Pediatric Issues

Compliance

- ▣ Cooperation
- ▣ Parental reluctance for daily meds if no sx's
- ▣ Nebulizer vs. MDI
 - Avoid “blow by”
- ▣ Holding chambers

Medications

- ▣ Intal MDI-N/A
- ▣ Oral SABA:
 - Side effects: sleep, behavior
- ▣ Theo:
 - Side effects
 - Therapeutic range
- ▣ Steroids
 - Decrease in rate of growth (2 cm)

Inhaled Corticosteroids

| Generic Name | Trade Name | Form | Dose | Freq | Age | Cost |
|----------------|------------|------------|-----------------------|--------|--------|-------------|
| Beclomethasone | Qvar | HFA | 40, 80 µg | bid | ≥5 yr | \$50-90 |
| Budesonide | Pulmicort | Neb | .25, .5, 1.0 mg | bid | ≥6 mo | \$90 to 190 |
| | generic | DPI | 90, 180 µg | | ≥6 yr | |
| Ciclesonide | Alvesco | HFA | 80, 160 µg | bid | ≥12 yr | \$70 |
| Fluticasone | Flovent | HFA DPI | 44, 110, 220 µg 50 | bid | ≥ 4 yr | \$44-82 |
| Mometasone | Asmanex | DPI | 110, 220 µg | Qd-bid | ≥4 yr | \$110-160 |



Combination: ICS+LABA

| Generic | Trade Name | Form | Dose | Freq | Age | Cost |
|--------------------------|-----------------------------|------------|-------------------------------------|------|-------|-------|
| Fluticasone + Salmeterol | Advair Diskus Advair HFA | DPI HFA | 100, 250, 500/50 45, 110, 230/21 | bid | ≥4 yr | \$200 |
| Mometasone + Formoterol | Dulera | HFA | 100, 200/5 | bid | ≥12 | \$230 |
| Budesonide + Formoterol | Symbicort | HFA | 80, 160/4.5 | bid | ≥5 yr | \$170 |



Inhaled Steroid: Risks vs. Benefits

- ▣ 1998: FDA labeled all INS and ICS with cautions re: growth reduction, glaucoma, cataracts, HPA axis, and immune suppression
- ▣ Studies
 - Cochrane Review
 - **Intermittent vs daily ICS for persistent asthma in children and adults, Dec 2012 (6 trials-4 peds, duration:12-52 wks)**
 - **Growth reduction: 4 mm; n=532**
 - **ICS is not associated with bone density reduction in children**
 - **Risk of cataracts is “negligible” in young asthmatics**
 - **Risk of glaucoma is “small” insufficient information**
 - **Risk of growth reduction; small and not sustained**

Summary



- ▣ Childhood wheezing:
 - Many causes; different phenotypes
- ▣ Triggers: smoke, viruses
 - <1 y/o: GER, anatomic
 - >1 y/o: Allergies
- ▣ Severity of asthma in early childhood
 - Determines later severity of symptoms and loss of lung function in later years
- ▣ Typical pattern for infants/pre-schoolers
 - Short recurrent cough/wheeze separated by symptom free intervals
- ▣ Inhaled steroid (over coming “steroid-phobia”)
 - first line treatment all ages
- ▣ Asthma visits
 - review inhaler technique, education, written action plan